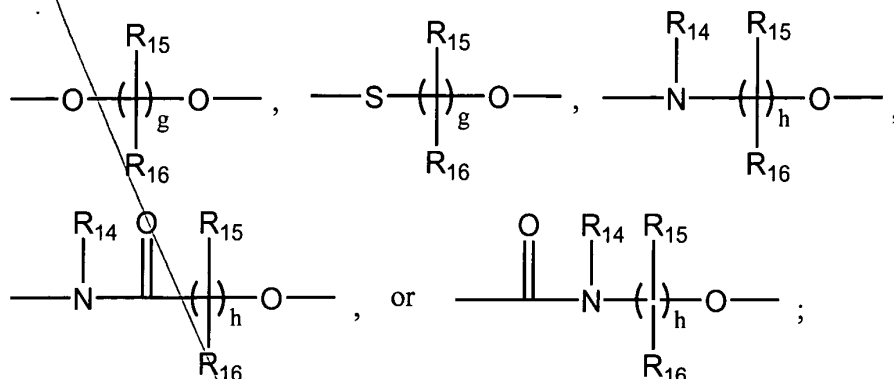


Q' out
Q' in

A is -O-, -S-, -SO-, -SO₂-, -NR₁₃-, -C(O)-, -N(R₁₄)C(O)-, -C(O)N(R₁₅)-,
-N(R₁₄)C(O)N(R₁₅)-, -C(R₁₄)=N-, a chemical bond,



B is -O-, -S-, -SO-, -SO₂-, -NR₁₇-, a chemical bond, ethynylene, -C(O)-,
-N(R₁₈)C(O)-, or -C(O)NR₁₈-;

D is -O-, -S-, -NR₁₉-, a chemical bond, ethynylene, -N(R₂₀)C(O)-, -C(O)-, or
-C(O)N(R₂₀)-;

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R₁, R₃, R₅, R₇, R₉, and R₁₁, are independently hydrogen, halogen, alkyl, carboxyl,
alkoxycarbonyl or aralkyl;

R₂, R₄, R₆, R₈, R₁₀ and R₁₂, are independently -(CH₂)_q-X;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl,
aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl,
alkoxycarbonyl, tetrazolyl, acyl, acylHNSO₂-, -SR₂₃, Y¹Y²N- or Y³Y⁴NCO-;

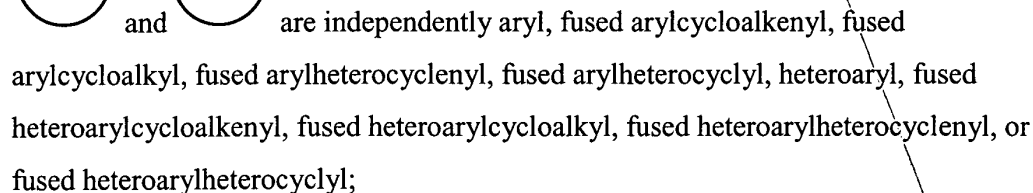
Y¹ and Y² are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of

Y¹ and Y² is hydrogen or alkyl and the other of Y¹ and Y² is acyl or aroyl;

at
aa'

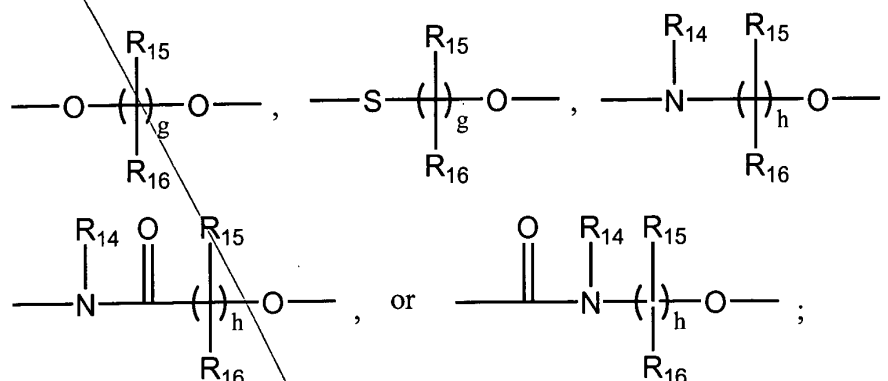
~~Y³ and Y⁴ are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;
Z is R₂₁O₂C-, R₂₁OC-, cyclo-imide, -CN, R₂₁O₂SHNCO-, R₂₁O₂SHN-, (R₂₁)₂NCO-,
R₂₁O- 2,4-thiazolidinedionyl, or tetrazolyl; and
R₂₁ is hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;
R₁₃, R₁₇, R₁₉ and R₂₃ are independently R₂₂OC-, R₂₂NHOC-, hydrogen, alkyl, aryl,
heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;
R₁₄, R₁₅, R₁₆, R₁₈ and R₂₀ are independently hydrogen, alkyl, aralkyl, carbonyl, or
alkoxycarbonyl;
or R₁₄, and R₁₅ taken together with the carbon and nitrogen atoms through which they
are linked form a 5 or 6-membered azaheterocyclyl group; or
when a is 2-4, then vicinal R₁ radicals taken together with the carbon atoms to which
the R₁ radicals are linked form an ethylene group; or
when b is 2-4, then vicinal R₃ radicals taken together with the carbon atoms to which
the R₃ radicals are linked form an ethylene group; or
when c is 2-4, then vicinal R₅ radicals taken together with the carbon atoms to which
the R₅ radicals are linked form an ethylene group; or
when d is 2-5, then vicinal R₇ radicals taken together with the carbon atoms to which
the R₇ radicals are linked form an ethylene group; or
when e is 2-4, then vicinal R₉ radicals taken together with the carbon atoms to which
the R₉ radicals are linked form an ethylene group; or
when f is 2-6, then vicinal R₁₁ radicals taken together with the carbon atoms to which
the R₁₁ radicals are linked form an ethylene group; and
R₂₂ is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or
aralkyl; or
a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a
solvate thereof.~~

27. (Amended) A compound of formula (Ia)



Int
CO²

A is -O-, -S-, -SO-, -SO₂-, -NR₁₃-, -C(O)-, -N(R₁₄)C(O)-, -C(O)N(R₁₅)-,
-N(R₁₄)C(O)N(R₁₅)-, -C(R₁₄)=N-, a chemical bond,



B is -O-, -S-, -SO-, -SO₂-, -NR₁₇-, a chemical bond, ethynylene, -C(O)-,
-N(R₁₈)C(O)-, or -C(O)NR₁₈-;

D is -O-, -S-, -NR₁₉-, a chemical bond, ethynylene, -N(R₂₀)C(O)-, -C(O)-, or
-C(O)N(R₂₀)-

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R₁, R₃, R₅, R₇, R₉, and R₁₁, are independently hydrogen, halogen, alkyl, carboxyl,
alkoxycarbonyl or aralkyl;

R₂, R₄, R₆, R₈, R₁₀ and R₁₂, are independently -(CH₂)_q-X;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl,
aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl,
alkoxycarbonyl, tetrazolyl, acyl, acylHNSO₂-, -SR₂₃, Y¹Y²N- or Y³Y⁴NCO-;

Y¹ and Y² are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of

Y¹ and Y² is hydrogen or alkyl and the other of Y¹ and Y² is acyl or aroyl;

9²
ant
AQ²

~~Y³ and Y⁴ are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;
Z is R₂₁O₂C-, R₂₁OC-, cyclo-imide, -CN, R₂₁O₂SHNCO-, R₂₁O₂SHN-, (R₂₁)₂NCO-,
R₂₁O- 2,4-thiazolidinedionyl, or tetrazolyl;
R' and R'' are ring system substituents;
R₂₁ is hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;
R₁₃, R₁₇, R₁₉ and R₂₃ are independently R₂₂OC-, R₂₂NHOC-, hydrogen, alkyl, aryl,
heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;
R₁₄, R₁₅, R₁₆, R₁₈ and R₂₀ are independently hydrogen, alkyl, aralkyl, carbonyl, or
alkoxycarbonyl;
or R₁₄, and R₁₅ taken together with the carbon and nitrogen atoms through which they
are linked form a 5 or 6-membered azaheterocyclyl group; or
when a is 2-4, then vicinal R₁ radicals taken together with the carbon atoms to which
the R₁ radicals are linked form an ethylene group; or
when b is 2-4, then vicinal R₃ radicals taken together with the carbon atoms to which
the R₃ radicals are linked form an ethylene group; or
when c is 2-4, then vicinal R₅ radicals taken together with the carbon atoms to which
the R₅ radicals are linked form an ethylene group; or
when d is 2-5, then vicinal R₇ radicals taken together with the carbon atoms to which
the R₇ radicals are linked form an ethylene group; or
when e is 2-4, then vicinal R₉ radicals taken together with the carbon atoms to which
the R₉ radicals are linked form an ethylene group; or
when f is 2-6, then vicinal R₁₁ radicals taken together with the carbon atoms to which
the R₁₁ radicals are linked form an ethylene group; and
R₂₂ is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or
aralkyl; or
a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a
solvate thereof.~~

31. (Amended) A compound according to claim 27 wherein

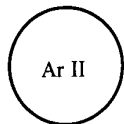
aa³

a = 1 or 2;

A is -O-;

b = 0;

R₁, R₂, R₇ and R₈ are independently hydrogen;



is optionally substituted phenyl;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen, halo or benzyloxy;

R'' is lower alkyl;

Z is -CO₂H.

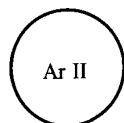
32. (Amended) A compound according to claim 27 wherein:

a = 1 or 2;

A is -O-;

b = 0;

R₁, R₂, R₅ and R₆ are independently hydrogen;



is optionally substituted phenyl;

c = 1;

B is -O-;

d = 0;

e = 0;

f = 0;

D and E are a chemical bond;

aa³
R' is hydrogen, halo or benzyloxy;

R'' is lower alkyl;

Z is -CO₂H.

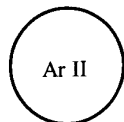
33. A compound according to claim 27 wherein:

a = 1 or 2;

A is -O-;

b = 0;

R₁, R₂, R₇, R₈, R₁₁ and R₁₂ are independently hydrogen;



is optionally substituted phenyl;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 1;

D and E are a chemical bond;

R' is halo;

R'' is lower alkyl;

Z is -CO₂H.

34. (Amended) A compound according to claim 27 wherein:

a = 1;

A is -O-;

b = 0;

c = 0-1;

B is -O-;

d = 0 or 1, wherein c+d = 1 or 2;

e = 0;

f = 0;

aa³
D and E are a chemical bond;
R' is hydrogen, aralkoxy, or halo;
R'' is lower alkyl;
Z is -CO₂H.

aa⁴
89. (New) A compound as claimed in claim 20, wherein the ring system substituent is selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, lower alkyl, branched alkyl, fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethyloxy.

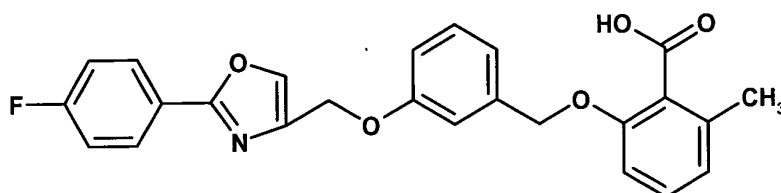
90. (New) A compound as claimed in claim 31, wherein R'' is methyl.

91. (New) A compound as claimed in claim 32, wherein R'' is methyl.

92. (New) A compound as claimed in claim 33, wherein R'' is methyl.

93. (New) A compound as claimed in claim 34, wherein R'' is methyl.

94. (New) A compound as claimed in claim 1, wherein the compound is



In the Abstract:

Please delete the current Abstract and replace it with the Abstract attached to the end of this Preliminary Amendment.